PATENT COOPERATION TREATY

C1037.70048WO00

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
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DOCKETED
APR 19 2005

Confirmation ☐ Initials
Docketing ☑ TC

06/14/05 ✓
05/14/05 NO Ext ✓
12/9/05 - after 12/19/04
TCL

PCT

WRITTEN OPINION

(PCT Rule 66)

Applicant's or agent's file reference C01037.70048 WO00	Date of Mailing (*day/month/year*) 14 APR 2005 REPLY DUE within 1 months/days from the above date of mailing

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US03/25935	19 August 2003 (19.08.2003)	19 August 2003 (19.08.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A01N 43/04; A61K 31/70; C07H 19/00, 21/00, 21/02, 21/04 and US Cl.: 514/44; 536/22.1, 23.1

Applicant

COELY PHARMACEUTICAL GROUP, INC.

1. This written opinion is the first (first, etc,) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 19 December 2005 (19.12.2005) ← 16 2004?

Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Dorothea Lawrence for Patricia A. Duffy Telephone No. 571.272.1600

Form PCT/IPEA/408 (cover sheet)(July 1998)

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International application No.
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I. Basis of the opinion

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed

☒ the description:
pages 1-125, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 126-138, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-46, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-90, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets~~/fig~~ NONE

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. Claims 5-11, 18-21 (not search in 210). Claims 22-27 are improper multiple dependent claims.

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 22-27 are so unclear that no meaningful opinion could be formed *(specify)*:

Claims 22-27 are multiply dependnet claims that depend from claims 12-17 that are also multiply dependent. As such these claims are improper multiple dependent claims under PCT Rule 6.4(a)

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 5-11 and 18-21.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	4	YES
	Claims	1-3 and 12-17	NO
Inventive Step (IS)	Claims	4	YES
	Claims	1-3 and 12-17	NO
Industrial Applicability (IA)	Claims	1-4 and 12-17	YES
	Claims	NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-3 and 12-16 lack novelty under PCT Article 33(2) as being anticipated by Hutcherson et al (US Patent 5,663,153 issued September 2, 1997).

Hutcherson et al teach SEQ ID NO:2 which is a phosphorothioate oligonucleotide analog 21 nucleotides in length that is immunostimulatory (column 9, line 15 - column 10, line 22) in that they stimulate IL-1 . The phosphorothioate analog of SEQ ID NO:2 comprises multiple internal pyrimidine-purine linkages and a chimeric backbone, wherein the chimeric back bone is composed of different dexoybases. That is the term "chimeric backbone" is broadly applied as not being the same repeating unit.

Claims 1-3 and 12-17 lack novelty under PCT Article 33(2) as being anticipated by Krieg et al (US Patent 6,214,806 issued April 10, 2001).

Krieg et al teach immunostimulatory nucleic acids comprising CpG dinucleotides wherein for use *in vivo*, nucleic acids are preferably relative resistant to degradation. Krieg et al teach that nucleic acid stabilization can be accomplished via phosphate backbone modifications. A preferred stabilized nucleic acid has at least a partial phosphorothioate modified backbone. (column 7, second full paragraph). As such, Krieg et al teach CpG immunostimulatory nucleic acids with chimeric phosphorothioate modified backbones. Krieg et al teach that the backbone modification can occur at the 5' end or at the 3' end at the last five nucleotides of the 3' end of the nucleic acid (column 8, lines 35-50). As such, SEQ ID NOS: 2, 4 and 5 meet this limitation, having the requisite Pyrimidine-purine internal to the nucleic acid sequence and are within the last five nucleotide of the 3' end of the oligonucleotide. As such, Krieg et al teaches the claimed invention when the phosphate backbone is chimeric, as opposed to the sugar backbone.

Claim 4, as limited to SEQ ID NO:1 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the sequence as immunostimulatory or backbone modification of this particular sequence.

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Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:
The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.